PSJ14 Janssen Opp Exh 23 – JAN-MS-00238346

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAR 30 2000

TRANSMITTED VIA FACSIMILE

Cynthia Chianese
Assistant Director
Regulatory Affairs
Janssen Pharmacuetica
1125 Trenton-Harbourton Road
P.O. Box 200
Titusville, NJ 08560-0200

RE: NDA 19-813
Duragesic (fentanyl transdermal system)
MACMIS ID #8664

Dear Ms. Chianese:

Reference is made to Janssen Pharmaceutica's (Janssen) letter, dated February 29, 2000, in response to a letter from the Division of Drug Marketing, Advertising, and Communications (DDMAC), dated February 15, 2000. Our letter concerned the alleged dissemination of "homemade" promotional pieces that promoted Duragesic (fentanyl transdermal system) capsules in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. We requested that you investigate the extent that these "homemade" pieces were used to promote Duragesic, the number of health care professionals who received these pieces, and that you provide the complete promotional pieces as they were allegedly disseminated.

In your letter, you described the circumstances in which the violative promotional materials were disseminated. Additionally, your letter commented on your policy for prohibiting dissemination of homemade materials by your sales force, and specified the corrective actions taken to ensure that this activity will not continue.

We have reviewed the "homemade" promotional pieces and have determined that they are false or misleading because they contain misrepresentations of safety information, broaden Duragesic's indication, contain unsubstantiated claims, and lack fair balance. Specific examples include, but are not limited to, the following "homemade" promotional pieces:

December 9, 1999 Mailing – "The #1 Reason to convert your patients to the Duragesic Patch"

Misrepresentation of Safety Information

Promotional materials are false or misleading if they contain representations or suggestions that a drug's safety or effectiveness is comparable or superior to another drug when such has not been demonstrated by substantial evidence. Examples of your claims that misrepresent the safety profile for Duragesic include:

- You present the claim, "Significantly LESS constipation!" This claim suggests that Duragesic is associated with significantly less constipation than other available opioids. However, this claim has not been demonstrated by substantial evidence. Therefore, without supporting substantial evidence, this claim is false or misleading. Furthermore, this claim misrepresents the safety profile for Duragesic because it minimizes the risk of constipation that is associated with Duragesic therapy. Please refer to our untitled letter to Janssen, dated March 5, 1998, addressing this issue.

- You present the claim, "Low abuse potential!" This claim suggests that Duragesic has less potential for abuse than other currently available opioids. However, this claim has not been demonstrated by substantial evidence. Furthermore, this claim is contradictory to information in the approved product labeling (PI) that states, "Fentanyl is a Schedule II controlled substance and can produce drug dependence similar to that produced by morphine." Therefore, this claim is false or misleading.

Broadening of indication

Promotional materials are misleading if they contain a representation or suggestion that a drug is more useful in a broader range of conditions or patients than has been demonstrated by substantial evidence.

- You present the claim, "It's not just for end stage cancer anymore!" This claim suggests that Duragesic can be used for any type of pain management. However, the PI for Duragesic states, "Duragesic (fentanyl transdermal system) is indicated in the management of chronic pain in patients who require continuous opiod analgesia for pain that cannot be managed by lesser means...." Therefore, the suggestion that Duragesic can be used for any type of pain management promotes Duragesic's for a much broader use than is recommended in the PI, and thus, is misleading. In addition, the suggestion that Duragesic can be used to treat any kind of pain is contradictory to the boxed warning in the PI. Specifically the PI sates,

  BECAUSE SERIOUS OR LIFE-THREATENING HYPOVENTILATION COULD OCCUR, DURAGESIC® (FENTANYL TRANSDERMAL SYSTEM) IS CONTRAINDICATED:

[redacted]

- In the management of acute or post-operative pain, including use in out-patient surgeries....

Unsubstantiated Claims

You present several unsubstantiated claims for Duragesic throughout this "homemade" promotional piece. Examples of your unsubstantiated claims include:

- You present the claim, "Preferred regimen: 2 x per week versus 2 x per day!" This claim suggests that patients prefer Duragesic to other available oral opioids that are taken twice daily. However, this patient preference claim is not supported by substantial evidence. Therefore, we consider this claim false or misleading.

- You present the claim, "Easy for Patient Compliance." This claim suggests that Duragesic may enhance patient compliance when compared to other opioids. However, this claim is not supported by specific compliance data, and therefore, is false or misleading.

- You present quality of life claims, including but not limited to, "And the #1 reason to convert your patients to the Duragesic patch: QUALITY OF LIFE," and "...without pain, patient's sleep better, increase daily activities, and spend more quality time with their families." Health related quality of life claims such as these require substantial supporting evidence in the form of adequate and well-controlled studies designed to specifically assess these outcomes. Therefore, without substantiation from adequate studies, the claims presented in this "homemade" promotional piece are misleading,

Fair Balance

Promotional materials must present information relating to the contraindications, warnings, precautions, and side effects with a prominence and readability reasonably comparable to the presentation of information relating to the effectiveness of the product. This "homemade" promotional piece is lacking in fair balance with respect to the content and presentation of risk information related to the use of Duragesic.

- Although this piece contains numerous claims for the efficacy and safety of Duragesic, **you have not presented any risk information** concerning the boxed warnings, contraindications, warnings, precautions, or side effects associated with Duragesic's use (emphasis added). Therefore, this promotional piece is lacking in fair balance, or otherwise misleading, because it fails to address important risks and restrictions associated with Duragesic therapy.

Monthly Cost of Therapy (30 Days)

Misrepresentation of Safety Information

- Your present the claim, "Duragesic results in **much less Constipation** compared to Oxycontin (Senokot $1.00/day). However, this comparative claim to Oxycontin is not supported by substantial evidence. Therefore, this unsubstantiated superiority claim is false or misleading. Furthermore, this claim minimizes the risk of constipation that is associated with Duragesic therapy.

Cost Comparison

- You present a table that compares the price of different strengths of Duragesic and Oxycontin from eight retail pharmacies. This table is followed by the claim that "Duragesic is marginally less expensive." However, this comparison is misleading because it implies that Duragesic is equally safe, effective, and interchangeable with Oxycontin for the doses compared. Furthermore, this cost information lacks substantiation and does not provide a reference as to the source of the cost information presented.

Failure to Submit

- Promotional materials must be submitted to the FDA under Form FDA 2253 at the time of initial dissemination. However, our records indicate these promotional materials were not submitted at the time of initial use.

We have reviewed your response and actions taken in response to the dissemination of this violative promotional piece. We do not wish to comment on your internal processes, however we do acknowledge your investigation and the corrective actions taken to prevent reoccurrence of this type of violative promotional activity. At this time we have no further questions and consider the matter regarding the "homemade" promotional pieces described in this letter to be closed.

However, you should immediately cease distribution of all other promotional materials for Duragesic that contain the same or similar claims or presentations. You should submit a written response to us on or before April 13, 2000, describing your intent and plans to comply with the above. Your letter should include a list of materials discontinued and the date on which these materials were discontinued.

If you have any further questions or comments, please contact me by facsimile at (301) 594-6771, or by writing at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondence regarding this matter, please refer to the MACMIS # 8664 and the NDA number.

Sincerely,

/S/

Spencer Salis, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications

DURAGESIC

entanyl Transdermal System

Top 10 List

Reasons to Switch Your Patients to the Duragesic Patch:

#10	It's not just for end stage cancer anymore!
#9	DURAGESIC - the LONGEST acting opioid!
#8	Significantly LESS constipation!
#7	EASY to Titrate - Remember the 6-30-60 rule!
#6	Cost Effective
#5	No clock watching as with oral opioids!
#4	Preferred regimen: 2 x per week versus 2 x per day!
#3	Low abuse potential!
#2	EASY for Patient Compliance

And the #1 reason to convert your patients to the Duragesic patch:

#1 QUALITY OF LIFE

Duragesic gives patients the FREEDOM to enjoy their lives without focus on their pain. And without pain, patients sleep better, increase daily activities, and spend more quality time with their families. They may even find time to stop and smell the flowers!

Our Top 10 List is complete, and now you know just how much your patients with chronic non-malignant pain can benefit from Duragesic. With these seeds, enjoy the blooms of your newly planted habit of writing Duragesic.

The New Standard in the New Millennium
For Chronic Non-Malignant Pain

[redacted]

[redacted]-HARBOURTON ROAD

Monthly Cost of Therapy (30 Days)

	Duragesic 25mcg	Oxycontin 20mg	Duragesic 50mcg	Oxycontin 40mg	Duragesic 75mcg	Oxycontin 80mg	Duragesic 100mcg
Target	119.38	155.39	181.38	256.69	281.98	402.99	347.98
Publix	127.78	139.39	183.78	246.99	287.98	450.99	357.98
Walmart	133.92	141.88	213.24	247.63	331.08	461.21	407.68
Perkins	139.14	156.88	209.86	266.24	326.8	486.82	403.28
Medicine Shoppe	125.78	136.89	191.78	238.89	299.78	590.89	371.78
Eckerds	162.58	149.59	217.38	254.69	347.98	485.19	399.78
Walgreens	135.98	132.95	209.98	235.97	323.98	447.95	405.98
Pill Box	128.00	137.40	198.00	237.00	308.00	450.00	360.00
Avg Cost	134	144	201	248	313	472	382

Duragesic results in ***much less Constipation*** compared to Oxycontin (Senokot $1.00/day)
Duragesic is marginally less expensive.

Attachment II